IAPO1 Record CT/PTO 26 SEP 2006

SEQUENCE LISTING

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<120> Immunoglobulins

<130> PB60806

<140> PCT/GB2005/001147

<141> 2005-03-29

<150> GB 0407197.3

<151> 2004-03-30

<150> GB 0407193.2

<151> 2004-03-30

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<170> PatentIn version 3.1

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Ser Leu Ser Ile Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asn Tyr
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20

25

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Gly Val His Trp Val Arg Gln Ser Pro Gly Lys Gly Leu Glu Trp Leu 35 40 45

Gly Val Ile Trp Arg Gly Gly Ser Thr Asp Tyr Asn Ala Ala Phe Met 50 55 60

Ser Arg Leu Ser Ile Thr Lys Asp Asn Ser Arg Ser Gln Val Phe Phe 65 70 75 80

Lys Met Asn Ser Leu Gln Ala Asp Asp Thr Ala Ile Tyr Tyr Cys Ala 85 90 95

Lys Ser Pro Asn Ser Asn Phe Tyr Trp Tyr Phe Asp Val Trp Gly Thr 100 105 110

Gly Thr Thr Val Thr Val Ser Ser 115 120

<210> 8

<211> 106

<212> PRT

<213> Mus sp.

<400> 8

Gln Ile Val Leu Thr Gln Ser Pro Thr Ile Met Ser Ala Ser Pro Gly $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$

Glu Lys Val Thr Met Thr Cys Ser Gly Ser Ser Ser Val Ser Tyr Met 20 25 30

Tyr Trp Tyr Gln Glu Lys Pro Gly Ser Ser Pro Arg Leu Leu Ile Glu 35 40 45

Asp Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser Gly Ser 50 55 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Arg Met Glu Ala Glu 65 70 75 80

Asp Ala Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Tyr Pro Pro Thr 85 90 95

Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys 100 105

<210> 9

<211> 120

<212> PRT

<213> Artificial sequence

<220>

<223> VH domain (humanised, B3)

<400> 9

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Leu Thr Asn Tyr 20 25 30

Gly Val His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 35 40 45

Ala Val Ile Trp Arg Gly Gly Ser Thr Asp Tyr Asn Ala Ala Phe Met 50 60

Ser Arg Phe Thr Ile Ser Lys Asp Asn Ser Lys Asn Thr Leu Tyr Leu 65 70 75 80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala 85 90 95

Lys Ser Pro Asn Ser Asn Phe Tyr Trp Tyr Phe Asp Val Trp Gly Arg 100 105 110

Gly Thr Leu Val Thr Val Ser Ser 115 120 <210> 10

<211> 106

<212> PRT

<213> Artificial sequence

<220>

<223> VL domain (humanised, L2)

<400> 10

Glu Arg Ala Thr Leu Ser Cys Ser Gly Ser Ser Ser Val Ser Tyr Met 20 25 30

Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Glu 35 40 45

Asp Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser 50 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Asn Leu Glu Pro Glu 65 70 75 80

Asp Phe Ala Val Tyr Tyr Cys Gln Gln Trp Ser Ser Tyr Pro Pro Thr 85 90 95

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys 100 105

<210> 11

<211> 450

<212> PRT

<213> Artificial sequence

<220>

<223> Heavy chain (humanised)

<400> 11

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Leu Thr Asn Tyr 20 25 30

Gly Val His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 35 40 45

Ala Val Ile Trp Arg Gly Gly Ser Thr Asp Tyr Asn Ala Ala Phe Met 50 60

Ser Arg Phe Thr Ile Ser Lys Asp Asn Ser Lys Asn Thr Leu Tyr Leu 65 70 75 80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala 85 90 95

Lys Ser Pro Asn Ser Asn Phe Tyr Trp Tyr Phe Asp Val Trp Gly Arg 100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val 115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala 130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser 145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val
165 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro 180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys 195 200 205

| Pro | Ser 210 | Asn | Thr | Lys | Val | Asp 215 | Lys | Lys | Val | Glu | Pro 220 | Lys | Ser | Cys | Asp |
|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|------------|
| Lys 225 | Thr | His | Thr | Cys | Pro 230 | Pro | Суз | Pro | Ala | Pro 235 | Glu | Leu | Leu | Gly | Gly 240 |
| Pro | Ser | Val | Phe | Leu 245 | Phe | Pro | Pro | Lys | Pro 250 | Lys | Asp | Thr | Leu | Met 255 | Ile |
| Ser | Arg | Thr | Pro 260 | Glu | Val | Thr | Суз | Val 265 | Val | Val | Asp | Val | Ser 270 | His | Glu |
| Asp | Pro | Glu 275 | Val | Lys | Phe | Asn | Trp 280 | Tyr | Val | Asp | Gly | Val 285 | Glu | Val | His |
| Asn | Ala 290 | Lys | Thr | Lys | Pro | Arg 295 | Glu | Glu | Gln | Tyr | Asn 300 | Ser | Thr | Tyr | Arg |
| Val 305 | Val | Ser | Val | Leu | Thr 310 | Val | Leu | His | Gln | Asp 315 | Trp | Leu | Asn | ,Gly | Lys 320 |
| Glu | Tyr | Lys | Cys | Lys 325 | Val | Ser | Asn | Lys | Ala 330 | Leu | Pro | Ala | Pro | Ile 335 | Glu |
| Lys | Thr | Ile | Ser 340 | Lys | Ala | Lys | Gly | Gln 345 | Pro | Arg | Glu | Pro | Gln 350 | Val | Tyr |
| Thr | Leu | Pro 355 | Pro | Ser | Arg | Asp | Glu 360 | Leu | Thr | Lys | Asn | Gln 365 | Val | Ser | Leu |
| | 370 | | | | | Phe 375 | | | | | 380 | | | | _ |
| 385 | | | | | 390 | Glu | | | | 395 | | | | | 400 |
| Leu | Asp | Ser | Asp | Gly 405 | Ser | Phe | Phe | Leu | Tyr 410 | Ser | Lys | Leu | Thr | Val 415 | Asp |
| Lys | Ser | Arg | Trp 420 | Gln | Gln | Gly | Asn | Val 425 | Phe | Ser | Cys | Ser | Val 430 | Met | His |

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro 435 440 445

Gly Lys 450

<210> 12

<211> 213

<212> PRT

<213> Artificial sequence

<220>

<223> Light chain (humanised)

<400> 12

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$

Glu Arg Ala Thr Leu Ser Cys Ser Gly Ser Ser Ser Val Ser Tyr Met 20 25 30

Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Glu 35 40 45

Asp Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser 50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Asn Leu Glu Pro Glu 65 70 75 80

Asp Phe Ala Val Tyr Tyr Cys Gln Gln Trp Ser Ser Tyr Pro Pro Thr 85 90 95

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Thr Val Ala Ala Pro 100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr 115 120 125 Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys 130 135 140

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu 145 150 155 160

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser 165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala 180 185 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe 195 200 205

Asn Arg Gly Glu Cys 210

<210> 13

<211> 252

<212> PRT

<213> Homo sapiens

<400> 13

Met Gly Val Leu Leu Thr Gln Arg Thr Leu Leu Ser Leu Val Leu Ala 1 5 10 15

Leu Leu Phe Pro Ser Met Ala Ser Met Ala Ala Ile Gly Ser Cys Ser 20 25 30

Lys Glu Tyr Arg Val Leu Leu Gly Gln Leu Gln Lys Gln Thr Asp Leu 35 40 45

Met Gln Asp Thr Ser Arg Leu Leu Asp Pro Tyr Ile Arg Ile Gln Gly 50 55 60

Leu Asp Val Pro Lys Leu Arg Glu His Cys Arg Glu Arg Pro Gly Ala 65 70 75 80

Phe Pro Ser Glu Glu Thr Leu Arg Gly Leu Gly Arg Arg Gly Phe Leu 85 90 95

Gln Thr Leu Asn Ala Thr Leu Gly Cys Val Leu His Arg Leu Ala Asp 100 105 110

Leu Glu Gln Arg Leu Pro Lys Ala Gln Asp Leu Glu Arg Ser Gly Leu 115 120 125

Asn Ile Glu Asp Leu Glu Lys Leu Gln Met Ala Arg Pro Asn Ile Leu 130 135 140

Gly Leu Arg Asn Asn Ile Tyr Cys Met Ala Gln Leu Leu Asp Asn Ser 145 150 155 160

Asp Thr Ala Glu Pro Thr Lys Ala Gly Arg Gly Ala Ser Gln Pro Pro 165 170 175

Thr Pro Thr Pro Ala Ser Asp Ala Phe Gln Arg Lys Leu Glu Gly Cys 180 185 190

Arg Phe Leu His Gly Tyr His Arg Phe Met His Ser Val Gly Arg Val 195 200 205

Phe Ser Lys Trp Gly Glu Ser Pro Asn Arg Ser Arg Arg His Ser Pro 210 215 220

His Gln Ala Leu Arg Lys Gly Val Arg Arg Thr Arg Pro Ser Arg Lys 225 230 235 240

Gly Lys Arg Leu Met Thr Arg Gly Gln Leu Pro Arg 245 250

<210> 14

<211> 759

<212> DNA

<213> Homo sapiens

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<210> 15

<211> 360

<212> DNA

<213> Mus sp.

<400> 15

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<210> 16

<211> 318

<213> Mus sp. <400> 16 caaattgttc tcacccagtc tccaacaatc atgtctgcat ctccagggga gaaggtcacc 60 atgacctgca gtggcagctc aagtgtaagt tacatgtatt ggtaccagga gaagccagga 120 tectececca gaetectgat tgaagacaca tecaaeetgg ettetggagt eeetgetege 180 ttcagtggca gtgggtctgg gacctcttac tctctcacaa tcagccgaat ggaggctgaa 240 gatgctgcca cttattactg tcaacagtgg agtagttatc cacccacgtt cggctcgggg 300 acaaagttgg aaatcaaa 318 <210> 17 <211> 360 <212> DNA <213> Artificial sequence <220> <223> VH domain (humanised, PN, B3) <400> 17 caggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60 tcctgtgcag cgtctggatt ctcattaact aattatggtg tacactgggt ccgccaggct 120 ccaggcaagg ggctggagtg ggtggcagtg atatggagag gtggaagcac agactacaat 180 gcagctttca tgtcccgatt caccatctcc aaggacaatt ccaagaacac gctgtatctg 240 caaatgaaca gcctgagagc cgaggacacg gctgtgtatt actgtgcgaa aagtccgaat 300 agtaactttt actggtattt cgatgtctgg ggccgtggca cactagtcac agtctcctca 360

<213> Artificial sequence

<210> 18

<211> 318

<212> DNA

<212> DNA

<220> <223> VL domain (humanised, PN, L2) <400> 18 gaaattgtgt tgacacagtc tccagccacc ctgtctttgt ctccagggga aagagccacc 60 ctctcctgca gtggcagctc aagtgtaagt tacatgtatt ggtaccaaca gaaacctggc 120 caggeteeca ggeteeteat egaagacaca tecaacetgg ettetggeat eecageeagg 180 ttcagtggca gtgggtctgg gacagactac actctcacca tcagcaacct agagcctgaa 240 gattttgcag tttattactg tcaacagtgg agtagttatc cacccacgtt tggccagggg 300 accaagctgg agatcaaa 318 <210> 19 <211> 1350 <212> DNA <213> Artificial sequence <220> <223> Heavy chain (humanised, PN) <400> 19 caggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc 60 tectgtgcag egtetggatt eteattaact aattatggtg tacaetgggt eegeeagget 120 ccaggcaagg ggctggagtg ggtggcagtg atatggagag gtggaagcac agactacaat 180 gcagctttca tgtcccgatt caccatctcc aaggacaatt ccaagaacac gctgtatctg 240 caaatgaaca gcctgagagc cgaggacacg gctgtgtatt actgtgcgaa aagtccgaat 300 agtaactttt actggtattt cgatgtctgg ggccgtggca cactagtcac agtctcctca 360 gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 420 ggcacagcgg ccctgggctg cctggtcaag gactacttcc ccgaaccggt gacggtgtcg 480 tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 540 ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 600

tacatctgca acgtgaatca caagcccagc aacaccaagg tggacaagaa agttgagccc

660

| aaatcttgtg | acaaaactca | çacatgccca | ccgtgcccag | cacctgaact | cctgggggga | 720 |
|------------|------------|------------|------------|------------|------------|------|
| ccgtcagtct | tcctcttccc | cccaaaaccc | aaggacaccc | tcatgatctc | ccggacccct | 780 |
| gaggtcacat | gcgtggtggt | ggacgtgagc | cacgaagacc | ctgaggtcaa | gttcaactgg | 840 |
| tacgtggacg | gcgtggaggt | gcataatgcc | aagacaaagc | cgcgggagga | gcagtacaac | 900 |
| agcacgtacc | gtgtggtcag | cgtcctcacc | gtcctgcacc | aggactggct | gaatggcaag | 960 |
| gagtacaagt | gcaaggtctc | caacaaagcc | ctcccagccc | ccatcgagaa | aaccatctcc | 1020 |
| aaagccaaag | ggcagccccg | agaaccacag | gtgtacaccc | tgcccccatc | ccgggatgag | 1080 |
| ctgaccaaga | accaggtcag | cctgacctgc | ctggtcaaag | gcttctatcc | cagcgacatc | 1140 |
| gccgtggagt | gggagagcaa | tgggcagccg | gagaacaact | acaagaccac | gcctcccgtg | 1200 |
| ctggactccg | acggctcctt | cttcctctac | agcaagctca | ccgtggacaa | gagcaggtgg | 1260 |
| cagcagggga | acgtcttctc | atgctccgtg | atgcatgagg | ctctgcacaa | ccactacacg | 1320 |
| cagaagagcc | tctccctgtc | tccgggtaaa | | | | 1350 |

<210> 20

<211> 639

<212> DNA

<213> Artificial sequence

<220>

<223> Light chain (humanised, PN)

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| agtgtcacag agcaggacag caaggacagc acctacagcc tcagcagcac cctgacgctg | | | | | | | | |
|---|--|--|--|--|--|--|--|--|
| agcaaagcag actacgagaa acacaaagtc tacgcctgcg aagtcaccca tcagggcctg | | | | | | | | |
| agctcgcccg tcacaaagag cttcaacagg ggagagtgt | | | | | | | | |
| <210> 21 | | | | | | | | |
| <211> 120 | | | | | | | | |
| <212> PRT | | | | | | | | |
| <213> Artificial sequence | | | | | | | | |
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| <220> | | | | | | | | |
| <223> VH domain (B4, humanised) | | | | | | | | |
| <400> 21 | | | | | | | | |
| Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg 1 5 10 15 | | | | | | | | |
| Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Leu Thr Asn Tyr 20 25 30 | | | | | | | | |
| Gly Val His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 35 40 . 45 | | | | | | | | |
| Ala Val Ile Trp Arg Gly Gly Ser Thr Asp Tyr Asn Ala Ala Phe Met 50 55 60 | | | | | | | | |
| Ser Arg Leu Thr Ile Ser Lys Asp Asn Ser Lys Asn Thr Leu Tyr Leu 65 70 75 80 | | | | | | | | |
| Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala 85 90 95 | | | | | | | | |
| Lys Ser Pro Asn Ser Asn Phe Tyr Trp Tyr Phe Asp Val Trp Gly Arg 100 105 110 | | | | | | | | |
| Gly Thr Leu Val Thr Val Ser Ser 115 120 | | | | | | | | |

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<210> 22
<211> 37
<212> DNA
<213> Artificial sequence
<220>
<223> VH forward primer
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<210> 23
<211> 28
<212> DNA
<213> Artificial sequence
<220>
<223> VH reverse primer
gatggactag tgtccctgtg ccccagac
                                                                     28
<210> 24
<211> 37
<212> DNA
<213> Artificial sequence
<220>
<223> VL forward primer
<400> 24
gatgaagctt gccaccatgg attttcaggt gcagatt
                                                                     37
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<210> 25

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<211> 31
<212> DNA
<213> Artificial sequence
<220>
<223> VL reverse primer
<400> 25
gatgcgtacg tttgatttcc aactttgtcc c
<210> 26
<211> 124
<212> PRT
<213> Homo sapiens
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Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Gly Ser Ile Ser Ser Tyr
Tyr Trp Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile
Gly Tyr Ile Tyr Tyr Ser Gly Ser Thr Asn Tyr Asn Pro Ser Leu Lys
Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Phe Ser Leu
                                        75
Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala
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90

Arg Ser Pro Ser Ser Gly Ser Tyr Tyr Tyr Tyr Tyr Tyr Gly Met Asp

105

85

100

31

Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser 115 120

<210> 27

<211> 121

<212> PRT

<213> Homo sapiens

<400> 27

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr 20 25 30

Gly Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 35 40 45

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys 85 90 95

Ala Arg Asp Leu Gly Gly Pro Leu Tyr Trp Tyr Phe Asp Leu Trp Gly 100 105 110

Arg Gly Thr Leu Val Thr Val Ser Ser 115 120

<210> 28

<211> 106

<212> PRT

<213> Homo sapiens

<400> 28

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Lys Tyr 20 25 30

Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile 35 40 45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly 50 55 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Asn Leu Glu Pro 65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp Pro Pro 85 90 95

Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile 100 105

<210> 29

<211> 116

<212> PRT

<213> Artificial sequence

<220>

<223> Humanised VH construct A1

<400> 29

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu 1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asn Tyr 20 25 30

Gly Val His Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile 35 40 45

Gly Val Ile Trp Arg Gly Gly Ser Thr Asp Tyr Asn Ala Ala Phe Met $50 \hspace{1.5cm} 55 \hspace{1.5cm} 60$

Ser Arg Val Thr Ile Ser Val Asp Thr Ser Lys Asn Gln Val Ser Leu 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala 85 90 95

Lys Ser Pro Asn Ser Asn Phe Tyr Trp Tyr Phe Asp Val Trp Gly Gln 100 105 110

Gly Thr Thr Ser 115

<210> 30

<211> 116

<212> PRT

<213> Artificial sequence

<220>

<223> Humanised VH construct A2

<400> 30

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu
1 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asn Tyr 20 25 30

Gly Val His Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile 35 40 45

Gly Val Ile Trp Arg Gly Gly Ser Thr Asp Tyr Asn Ala Ala Phe Met 50 55 60

Ser Arg Val Thr Ile Ser Lys Asp Thr Ser Lys Asn Gln Val Ser Leu 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala 85 90 95

Lys Ser Pro Asn Ser Asn Phe Tyr Trp Tyr Phe Asp Val Trp Gly Gln 100 105 110

Gly Thr Thr Ser 115

<210> 31

<211> 116

<212> PRT

<213> Artificial sequence

<220>

<223> Humanised VH construct A3

<400> 31

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu 1 5 10 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asn Tyr 20 25 30

Gly Val His Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile 35 40 45

Gly Val Ile Trp Arg Gly Gly Ser Thr Asp Tyr Asn Ala Ala Phe Met 50 55 60

Ser Arg Val Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu 65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala 85 90 95

Lys Ser Pro Asn Ser Asn Phe Tyr Trp Tyr Phe Asp Val Trp Gly Gln 100 105 110

Gly Thr Thr Ser 115

<210> 32

<211> 116

<212> PRT

<213> Artificial sequence

<220>

<223> Humanised VH construct A4

<400> 32

Gln Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Glu 1 5 10 $^{\circ}$ 15

Thr Leu Ser Leu Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asn Tyr 20 25 30

Gly Val His Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Ile 35 40 45

Gly Val Ile Trp Arg Gly Gly Ser Thr Asp Tyr Asn Ala Ala Phe Met $50 \hspace{1.5cm} 55 \hspace{1.5cm} 60$

Ser Arg Leu Thr Ile Ser Lys Asp Asn Ser Lys Asn Gln Val Ser Leu 65 70 75 80

Lys Leu Ser Ser Val Thr Ala Ala Asp Thr Ala Val Tyr Tyr Cys Ala 85 90 95

Lys Ser Pro Asn Ser Asn Phe Tyr Trp Tyr Phe Asp Val Trp Gly Gln 100 105 110

Gly Thr Thr Ser 115 <210> 33

<211> 116

<212> PRT

<213> Artificial sequence

<220>

<223> Humanised VH construct B1

<400> 33

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Leu Thr Asn Tyr 20 25 30

Gly Val His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 35 40 45

Ala Val Ile Trp Arg Gly Gly Ser Thr Asp Tyr Asn Ala Ala Phe Met 50 60

Ser Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu 65 70 75 80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala 85 90 95

Arg Ser Pro Asn Ser Asn Phe Tyr Trp Tyr Phe Asp Val Trp Gly Arg 100 105 110

Gly Thr Leu Val 115

<210> 34

<211> 116

<212> PRT

<213> Artificial sequence

<220>

<223> Humanised VH construct B2

<400> 34

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Leu Thr Asn Tyr 20 25 30

Gly Val His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 35 40 45

Ala Val Ile Trp Arg Gly Gly Ser Thr Asp Tyr Asn Ala Ala Phe Met 50 60

Ser Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu 65 70 75 80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala 85 90 95

Lys Ser Pro Asn Ser Asn Phe Tyr Trp Tyr Phe Asp Val Trp Gly Arg 100 105 110

Gly Thr Leu Val 115

<210> 35

<211> 116

<212> PRT

<213> Artificial sequence

<220>

<223> Humanised VH construct B3

<400> 35

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg
1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Leu Thr Asn Tyr 20 25 30

Gly Val His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 35 40 45

Ala Val Ile Trp Arg Gly Gly Ser Thr Asp Tyr Asn Ala Ala Phe Met 50 60

Ser Arg Phe Thr Ile Ser Lys Asp Asn Ser Lys Asn Thr Leu Tyr Leu 65 70 75 80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala 85 90 95

Lys Ser Pro Asn Ser Asn Phe Tyr Trp Tyr Phe Asp Val Trp Gly Arg 100 105 110

Gly Thr Leu Val 115

<210> 36

<211> 116

<212> PRT

<213> Artificial sequence

<220>

<223> Humanised VH construct B4

<400> 36

Gln Val Gln Leu Val Glu Ser Gly Gly Gly Val Val Gln Pro Gly Arg 1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Leu Thr Asn Tyr 20 25 30

Gly Val His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 35 40 45

Ala Val Ile Trp Arg Gly Gly Ser Thr Asp Tyr Asn Ala Ala Phe Met 50 55 60

Ser Arg Leu Thr Ile Ser Lys Asp Asn Ser Lys Asn Thr Leu Tyr Leu 65 70 75 80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala 85 90 95

Lys Ser Pro Asn Ser Asn Phe Tyr Trp Tyr Phe Asp Val Trp Gly Arg 100 105 110

Gly Thr Leu Val 115

<210> 37

<211> 106

<212> PRT

<213> Artificial sequence

<220>

<223> Humanised VL construct L1

<400> 37

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Ser Gly Ser Ser Ser Val Ser Tyr Met $20 \hspace{1cm} 25 \hspace{1cm} 30$

Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr 35 40 45

Asp Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser 50 55 60

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Asn Leu Glu Pro Glu 65 70 75 80

Asp Phe Ala Val Tyr Tyr Cys Gln Gln Trp Ser Ser Tyr Pro Pro Thr 85 90 95

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys 100 105

<210> 38

<211> 106

<212> PRT

<213> Artificial sequence

<220>

<223> Humanised VL construct L2

<400> 38

Glu Ile Val Leu Thr Gln Ser Pro Ala Thr Leu Ser Leu Ser Pro Gly 1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Ser Gly Ser Ser Ser Val Ser Tyr Met 20 25 30

Tyr Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Glu 35 40 45

Asp Thr Ser Asn Leu Ala Ser Gly Ile Pro Ala Arg Phe Ser Gly Ser 50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Asn Leu Glu Pro Glu 65 70 75 80

Asp Phe Ala Val Tyr Tyr Cys Gln Gln Trp Ser Ser Tyr Pro Pro Thr 85 90 95

Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys 100 105

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<210> 39
<211> 19
<212> PRT
<213> Homo sapiens
<400> 39
Met Gly Trp Ser Cys Ile Ile Leu Phe Leu Val Ala Thr Ala Thr Gly
Val His Ser
<210> 40
<211> 5
<212> PRT
<213> Mus sp.
<400> 40
Asp Tyr Asn Met Asp
<210> 41
<211> 17
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<400> 41

<212> PRT

<213> Mus sp.

Asp Ile Asn Pro Asn Asn Gly Gly Thr Ile Asp Asn Gln Lys Phe Lys 1 $$ 5 $$ 10 $$ 15

Asp

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<211> 12
<212> PRT
<213> Mus sp.
<400> 42
<210> 43
<211> 10
<212> PRT
<213> Mus sp.
<400> 43
Ser Ala Thr Ser Ser Val Ser Val Met His
<210> 44
<211> 7
<212> PRT
<213> Mus sp.
<400> 44
Asp Thr Ser Lys Leu Ala Ser
<210> 45
<211> 9
<212> PRT
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<210> 42

<213> Mus sp.

<400> 45

<210> 46

<211> 121

<212> PRT

<213> Mus sp.

<400> 46

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala 1 5 10 15

Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Asp Tyr 20 25 30

Asn Met Asp Trp Val Lys Gln Ser His Gly Lys Lys Leu Glu Trp Ile
35 40 45

Gly Asp Ile Asn Pro Asn Asn Gly Gly Thr Ile Asp Asn Gln Lys Phe 50 60

Lys Asp Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr 65 70 75 80

Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Thr Ala Val Tyr Tyr Cys 85 90 95

Ala Arg Gly Ile Tyr Tyr Gly Ser His Tyr Phe Asp Tyr Trp Gly 100 105 110

Gln Gly Thr Thr Leu Thr Val Ser Ser 115 120

<210> 47

<211> 106

<212> PRT

<213> Mus sp.

<400> 47

Gln Ile Val Leu Thr Gln Ser Pro Ala Ile Met Ser Ala Ser Pro Gly $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$

Glu Lys Val Thr Met Thr Cys Ser Ala Thr Ser Ser Val Ser Val Met 20 25 30

His Trp Phe Gln Lys Lys Ser Gly Thr Ser Pro Lys Arg Trp Ile Tyr 35 40 45

Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Thr Arg Phe Ser Gly Ser 50 60

Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Ser Ser Met Glu Ala Glu 65 70 75 80

Asp Thr Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr 85 90 95

Phe Gly Ser Gly Thr Lys Leu Glu Leu Lys
100 105

<210> 48

<211> 121

<212> PRT

<213> Artificial sequence

<220>

<223> VH domain (humanised, B3)

<400> 48

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala 1 5 10 15 Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Asp Tyr 20 25 30

Asn Met Asp Trp Val Arg Gln Ala Pro Gly Gln Lys Leu Glu Trp Ile 35 40 45

Gly Asp Ile Asn Pro Asn Asn Gly Gly Thr Ile Asp Asn Gln Lys Phe 50 60

Lys Asp Arg Ala Thr Leu Thr Val Asp Lys Ser Thr Ser Thr Val Tyr 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys 85 90 95

Ala Arg Gly Ile Tyr Tyr Gly Ser His Tyr Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser 115 120

<210> 49

<211> 106

<212> PRT

<213> Artificial sequence

<220>

<223> VL domain (humanised, L2)

<400> 49

Glu Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly
1 5 10 15

Asp Arg Val Thr Ile Thr Cys Ser Ala Thr Ser Ser Val Ser Val Met 20 25 30

His Trp Phe Gln Lys Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr 35 40 45

Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser 50 55 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu 65 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr 85 90 95

Phe Gly Gly Gly Thr Lys Val Asp Ile Lys
100 105

<210> 50

<211> 451

<212> PRT

<213> Artificial sequence

<220>

<223> Heavy chain (humanised)

<400> 50

Glu Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ala 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe Thr Asp Tyr 20 25 30

Asn Met Asp Trp Val Arg Gln Ala Pro Gly Gln Lys Leu Glu Trp Ile $35 \hspace{1cm} 40 \hspace{1cm} 45$

Gly Asp Ile Asn Pro Asn Asn Gly Gly Thr Ile Asp Asn Gln Lys Phe 50 60

Lys Asp Arg Ala Thr Leu Thr Val Asp Lys Ser Thr Ser Thr Val Tyr 65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys 85 90 95

Ala Arg Gly Ile Tyr Tyr Gly Ser His Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser 115 120 Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala 135 Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val 150 Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala 165 170 Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val 180 Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys 215 Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly 235 Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met 245 250 Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His 260 265 Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val 275 280 285 His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr 290 295 Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly 305 310 315

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile 325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val 340 345 350

Tyr Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser 355 360 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu 370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro 385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val 405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met 420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser 435 440 445

Pro Gly Lys 450

<210> 51

<211> 213

<212> PRT

<213> Artificial sequence

<220>

<223> Light chain (humanised)

<400> 51

Glu Ile Val Leu Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Val Gly $1 \hspace{1cm} 5 \hspace{1cm} 10 \hspace{1cm} 15$

Asp Arg Val Thr Ile Thr Cys Ser Ala Thr Ser Ser Val Ser Val Met 20 25 30

His Trp Phe Gln Lys Lys Pro Gly Lys Ala Pro Lys Arg Trp Ile Tyr 35 40 45

Asp Thr Ser Lys Leu Ala Ser Gly Val Pro Ser Arg Phe Ser Gly Ser 50 60

Gly Ser Gly Thr Asp Tyr Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu 65 70 75 80

Asp Phe Ala Thr Tyr Tyr Cys Gln Gln Trp Ser Ser Asn Pro Leu Thr 85 90 95

Phe Gly Gly Thr Lys Val Asp Ile Lys Arg Thr Val Ala Ala Pro 100 105 110

Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr 115 120 125

Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys 130 135

Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu 145 150 155 160

Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser 165 170 175

Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala 180 185 190

Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser Phe 195 200 205

Asn Arg Gly Glu Cys 210

<210> 52

<211> 363

<212> DNA <213> Mus sp.

<400> 52
gaggtccagc tgcaacagtc tggacctgag ctggtgaagc ctggggcttc agtgaagata 60
tcctgcaagg cctctggata catattcact gactacaaca tggactgggt gaagcagagc 120
catggaaaga aacttgagtg gattggagat attaatccta ataatggtgg tactatcgac 180
aaccagaagt tcaaggacaa ggccacattg actgtagaca agtcctccag cacagcctac 240
atggagctcc gcagcctgac atctgaggac actgcagtct attactgtgc aagagggatt 300
tattactacg gtagtcacta ctttgactat tggggccaag gcaccactct cacagtctcc 360
tca

<210> 53

<211> 318

<212> DNA

<213> Mus sp.

<400> 53
caaattgttc tcacccagtc tccagcaatc atgtctgcat ctccagggga gaaggtcacc 60
atgacctgca gtgccacctc aagtgtaagt gtcatgcact ggttccagaa gaagtcaggt 120
acctcccca aaagatggat ttatgacaca tccaaactgg cttctggagt ccctactcgc 180
ttcagtggca gtgggtctgg gacctcttac tctctcacaa tcagtagcat ggaggctgaa 240
gatactgcca cttattactg ccagcagtgg agtagtaacc cactcacgtt cggttctggg 300
accaagctgg agctgaaa 318

<210> 54

<211> 363

<212> DNA

<213> Artificial sequence

<220> <223> VH domain (humanised, PN, B3) <400> 54 60 gaggtccagc tggtgcagtc tggggctgag gtgaagaagc ctggggcctc agtgaaggtt tcctgcaagg catctggata catattcacc gactacaaca tggactgggt gcgacaggcc 120 180 cctggacaaa aacttgagtg gattggagat attaatccta ataatggtgg tactatcgac 240 aaccagaagt tcaaggacag agccaccttg accgtagaca agtccacgag cacagtctac 300 atggagctga gcagcctgag atctgaggac acggccgtgt attactgtgc gagagggatt tattactacg gtagtcacta ctttgactat tggggccagg gaacactagt cacagtctcc 360 tca 363 <210> 55 <211> 318 <212> DNA <213> Artificial sequence <220> <223> VL domain (humanised, PN, L2) <400> gaaattgtgt tgacgcagtc tccatcctcc ctgtctgcat ctgttggaga cagagtcacc 60 atcacttgca gtgccacctc aagtgtaagt gtcatgcact ggttccagaa gaaaccaggg 120 aaagccccta agagatggat ctatgacaca tccaaactgg cttctggggt cccatcaagg 180 ttcagtggca gtggatctgg gacagattac actctcacca tcagcagtct gcaacctgaa 240 gattttgcaa cttattactg ccagcagtgg agtagtaacc cactcacgtt cggcggaggg 300 accaaagtgg atatcaaa 318 <210> 56 <211> 1353 <212> DNA <213> Artificial sequence

<223> Heavy chain (humanised, PN)

<400> 56 60 gaggtccagc tggtgcagtc tggggctgag gtgaagaagc ctggggcctc agtgaaggtt tcctgcaagg catctggata catattcacc gactacaaca tggactgggt gcgacaggcc 120 cctggacaaa aacttgagtg gattggagat attaatccta ataatggtgg tactatcgac 180 aaccagaagt tcaaggacag agccaccttg accgtagaca agtccacgag cacagtctac 240 atggagetga geageetgag atetgaggae aeggeegtgt attaetgtge gagagggatt 300 tattactacg gtagtcacta ctttgactat tggggccagg gaacactagt cacagtctcc 360 tcagcctcca ccaagggccc atcggtcttc cccctggcac cctcctccaa gagcacctct 420 gggggcacag cggccctggg ctgcctggtc aaggactact tccccgaacc ggtgacggtg 480 tegtggaaet caggegeeet gaecagegge gtgeacaeet teeeggetgt cetacagtee 540 tcaggactct actccctcag cagcgtggtg accgtgccct ccagcagctt gggcacccag 600 acctacatct gcaacgtgaa tcacaagccc agcaacacca aggtggacaa gaaagttgag 660 cccaaatctt gtgacaaaac tcacatgc ccaccgtgcc cagcacctga actcctgggg 720 ggaccgtcag tcttcctctt ccccccaaaa cccaaggaca ccctcatgat ctcccggacc 780 840 cctgaggtca catgcgtggt ggtggacgtg agccacgaag accctgaggt caagttcaac 900 tggtacgtgg acggcgtgga ggtgcataat gccaagacaa agccgcggga ggagcagtac aacagcacgt accgtgtggt cagcgtcctc accgtcctgc accaggactg gctgaatggc 960 aaggagtaca agtgcaaggt ctccaacaaa gccctcccag cccccatcga gaaaaccatc 1020 tecaaageea aagggeagee eegagaacea eaggtgtaca eeetgeeeee ateeegggat 1080 gagetgacea agaaceaggt cageetgace tgeetggtea aaggetteta teecagegae 1140 atcgccgtgg agtgggagag caatgggcag ccggagaaca actacaagac cacgcctccc 1200 gtgctggact ccgacggctc cttcttcctc tacagcaagc tcaccgtgga caagagcagg 1260 tggcagcagg ggaacgtett etcatgetee gtgatgcatg aggetetgea caaccactae 1320 acgcagaaga gcctctccct gtctccgggt aaa 1353

<211> 639 <212> DNA <213> Artificial sequence <220> <223> Light chain (humanised, PN) <400> 57 gaaattgtgt tgacgcagtc tccatcctcc ctgtctgcat ctgttggaga cagagtcacc 60 atcacttgca gtgccacctc aagtgtaagt gtcatgcact ggttccagaa gaaaccaggg 120 180 aaagccccta agagatggat ctatgacaca tccaaactgg cttctggggt cccatcaagg ttcagtggca gtggatctgg gacagattac actctcacca tcagcagtct gcaacctgaa 240 gattttgcaa cttattactg ccagcagtgg agtagtaacc cactcacgtt cggcggaggg 300 accaaagtgg atatcaaacg tacggtggct gcaccatctg tcttcatctt cccgccatct 360 420 gatgagcagt tgaaatctgg aactgcctct gttgtgtgcc tgctgaataa cttctatccc agagaggcca aagtacagtg gaaggtggac aacgccctcc aatcgggtaa ctcccaggag 480 agtgtcacag agcaggacag caaggacagc acctacagcc tcagcagcac cctgacgctg 540 agcaaagcag actacgagaa acacaaagtc tacgcctgcg aagtcaccca tcagggcctg 600 agctcgcccg tcacaaagag cttcaacagg ggagagtgt 639 <210> 58 <211> 37 <212> DNA <213> Artificial sequence <220> <223> VH forward primer <400> 58

37

<210> 59

gatgaagctt gccaccatgg gatggagctg ggtcttt

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<211> 37
<212> DNA
<213> Artificial sequence
<220>
<223> VL forward primer
<400> 59
                                                                    37
gatgaagctt gccaccatgg atttacaggt gcagatt
<210> 60
<211> 31
<212> DNA
<213> Artificial sequence
<220>
<223> VL reverse primer
<400> 60
gatgcgtacg tttcagctcc agcttggtcc c
                                                                    31
<210> 61
<211> 450
<212> PRT
<213> Artificial sequence
<220>
<223> Heavy chain (humanised, Fc mutated)
<400> 61
Gln Val Gln Leu Val Glu Ser Gly Gly Val Val Gln Pro Gly Arg
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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Ser Leu Thr Asn Tyr

25

20

Gly Val His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val Ala Val Ile Trp Arg Gly Gly Ser Thr Asp Tyr Asn Ala Ala Phe Met 55 Ser Arg Phe Thr Ile Ser Lys Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Lys Ser Pro Asn Ser Asn Phe Tyr Trp Tyr Phe Asp Val Trp Gly Arg 105 Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val 165 170 Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro 180 185 Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys 200 Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp 210 215 Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Ala Gly Ala 225 230

Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile

250

245

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu 260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His 275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg 290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys 305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu 325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr 340 345 350

Thr Leu Pro Pro Ser Arg Asp Glu Leu Thr Lys Asn Gln Val Ser Leu 355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp 370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val 385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp 405 410 415

Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His 420 425 430

Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro 435 440 445

Gly Lys 450

<210> 62

<211> 1350

<212> DNA

<213> Artificial sequence

<220>

<223> Heavy chain (humanised, Fc mutated, PN)

<400> 62 60 caggtgcagc tggtggagtc tgggggaggc gtggtccagc ctgggaggtc cctgagactc tcctgtgcag cgtctggatt ctcattaact aattatggtg tacactgggt ccgccaggct 120 ccaggcaagg ggctggagtg ggtggcagtg atatggagag gtggaagcac agactacaat 180 gcagctttca tgtcccgatt caccatctcc aaggacaatt ccaagaacac gctgtatctg 240 caaatgaaca gcctgagagc cgaggacacg gctgtgtatt actgtgcgaa aagtccgaat 300 agtaactttt actggtattt cgatgtctgg ggccgtggca cactagtcac agtctcctca 360 gcctccacca agggcccatc ggtcttcccc ctggcaccct cctccaagag cacctctggg 420 ggcacagegg ceetgggetg cetggtcaag gactacttee eegaaceggt gaeggtgteg 480 tggaactcag gcgccctgac cagcggcgtg cacaccttcc cggctgtcct acagtcctca 540 ggactctact ccctcagcag cgtggtgacc gtgccctcca gcagcttggg cacccagacc 600 tacatetgea aegtgaatea caageeeage aacaceaagg tggacaagaa agttgageee 660 aaatcttgtg acaaaactca cacatgccca ccgtgcccag cacctgaact cgcgggggca 720 cegteagtet teetetteee eccaaaacee aaggacacee teatgatete eeggaceeet 780 gaggtcacat gcgtggtggt ggacgtgagc cacgaagacc ctgaggtcaa gttcaactgg 840 tacgtggacg gcgtggaggt gcataatgcc aagacaaagc cgcgggagga gcagtacaac 900 agcacgtacc gtgtggtcag cgtcctcacc gtcctgcacc aggactggct gaatggcaag 960 gagtacaagt gcaaggtctc caacaaagcc ctcccagccc ccatcgagaa aaccatctcc 1020 aaagccaaag ggcagccccg agaaccacag gtgtacaccc tgcccccatc ccgggatgag 1080 ctgaccaaga accaggtcag cctgacctgc ctggtcaaag gcttctatcc cagcgacatc 1140 gccgtggagt gggagagcaa tgggcagccg gagaacaact acaagaccac gcctcccgtg 1200 ctggactccg acggctcctt cttcctctac agcaagctca ccgtggacaa gagcaggtgg 1260

cagcagggga acgtcttctc atgctccgtg atgcatgagg ctctgcacaa ccactacacg

1320

cagaagagcc tctccctgtc tccgggtaaa

<210> 63

<211> 252

<212> PRT

<213> Macaca fascicularis

<400> 63

Met Gly Val Pro Leu Thr Arg Arg Thr Leu Leu Ser Leu Ile Leu Ala 1 5 10 15

Leu Leu Phe Pro Ser Met Ala Ser Met Ala Ala Met Gly Ser Cys Ser 20 25 30

Lys Glu Tyr Arg Met Leu Leu Gly Gln Leu Gln Lys Gln Thr Asp Leu 35 40 45

Met Gln Asp Thr Ser Arg Leu Leu Asp Pro Tyr Ile Arg Ile Gln Gly 50 55 60

Leu Asp Ile Pro Lys Leu Arg Glu His Cys Arg Glu Ser Pro Gly Ala 65 70 75 80

Phe Pro Ser Glu Glu Thr Leu Arg Gly Leu Gly Arg Arg Gly Phe Leu 85 90 95

Gln Thr Leu Asn Ala Thr Leu Gly Cys Val Leu His Arg Leu Ala Asp 100 105 110

Leu Glu Gln His Leu Pro Lys Ala Gln Asp Leu Glu Arg Ser Gly Leu 115 120 125

Asn Ile Glu Asp Leu Glu Lys Leu Gln Met Ala Arg Pro Asn Val Leu 130 135 140

Gly Leu Arg Asn Asn Val Tyr Cys Met Ala Gln Leu Leu Asp Asn Ser 145 150 155 160

Asp Met Thr Glu Pro Thr Lys Ala Gly Arg Gly Thr Pro Gln Pro Pro 165 170 175

Thr Pro Thr Pro Thr Ser Asp Val Phe Gln Arg Lys Leu Glu Gly Cys
180 185 190

Ser Phe Leu Arg Gly Tyr His Arg Phe Met His Ser Val Gly Arg Ile 195 200 205

Phe Ser Lys Trp Gly Glu Ser Pro Asn Arg Ser Arg Arg His Ser Pro 210 215 220

His Gln Ala Leu Arg Lys Gly Val Arg Arg Thr Arg Pro Ser Arg Lys 225 230 235 240

Gly Asn Arg Leu Met Pro Arg Gly Gln Leu Pro Arg 245 250

<210> 64

<211> 759

<212> DNA

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